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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MARTIN D. MOYNIHAN d/b/a PRTSI, INC.
P.O. BOX 16446
ARLINGTON, VA 22215

EXAMINER	
VANDERVEGT, FRANCOIS P	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
12/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/075,257	REITER, YORAM	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20080910, 20081120, 20080501*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of U.S. Application Serial Number 09/534,966.

Claims 1-20 and 35 have been canceled.

Claims 21-34 are currently pending and are the subject of examination in the present Office Action.

1. In view of Applicant's amendment filed June 12, 2008 no outstanding ground of rejection is maintained. The following represents a new ground of rejection necessitated by Applicant's amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 21-27 and 29-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Altman et al (Proc. Nat. Acad. Sci. (USA) [1993] 90:10330-10334; of record) in view of Mottez et al (J. Exp. Med. [1995] 181:493-502; U on form PTO-892, of record) and Mage et al (Proc. Nat. Acad. Sci. (USA) [1992] 89:10658-10662; 1 on form PTO-1449 filed 11/20/2008, newly cited).

Altman teaches a method for the production of soluble functional MHC class II complexes in *E. coli* (see entire document). Altman teaches the purification of MHC class II from inclusion bodies and the in vitro refolding of the MHC molecules. Altman teaches the association of the MHC molecules with antigenic peptides. Altman teaches that no other proteins are required for the efficient folding of the MHC molecules and that carbohydrate modification is not necessary for T cell recognition. Altman teaches that production in *E. coli* provides large quantities of MHC molecules needed for conformational and functional studies (page 10334 in particular). Altman teaches that production of empty MHC class I molecules is possible, but is inhibited by the instability of the complex at physiological temperatures (page 10334 in particular).

Altman teaches the purification of complexes including the use of size-exclusion chromatography i (page 10331, column 2 in particular) [claim 22].

Altman teaches denaturation of the inclusion bodies by standard methods (page 10330, column 2 in particular) [claim 26].

Altman teaches reduction of the MHC molecule prior to refolding (page 10331, column 1 in particular) [claim 29].

Altman teaches refolding under renaturation conditions, including oxidized glutathione and arginine (page 10331, column 1 and Figure 1 in particular) [claims 30-34].

Altman does not specifically teach the production of MHC class I molecules or single chain MHC molecules.

Mottez teaches single chain constructs comprising a murine MHC class I heavy chain joined to β_2-microglobulin with a covalently bound antigenic peptide. Mottez teaches that linker, or spacer, sequences separate the segments (see entire document) and allow the proper folding of the MHC class I domains and the peptide. Because the antigenic peptide is attached to the MHC class I molecule, it is constitutively produced in the same cell as the MHC class I molecule [claims 23, 25, 27].

The combined references do not teach placing the β_2m N-terminal to the MHC class I heavy chain portion of the construct.

Mage teaches the manufacture of a functional recombinant, soluble, single-chain MHC class I complex molecule that comprises the β_2m joined at its C-terminus via a linker peptide to the N-terminus of an MHC class I heavy chain sequence (Abstract, Figure 1, and paragraph bridging pages 10658-10659 in particular).

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to use the method of Altman to produce the single chain MHC class I molecule of Mottez in *E. coli*. The artisan would have been motivated with a reasonable expectation of success to place the β_2m either upstream or downstream of the MHC class I heavy chain portion of the construct by the showings of Mage and Mottez that either orientation results in a biologically functional soluble MHC class I complex. One would further have been motivated to combine the teachings with a reasonable expectation of success by the teaching of Altman that MHC molecules do not need accessory molecules for folding and that they do not need glycosylation to be functional. One would have been further motivated by the teaching of Altman that MHC class I molecules are stable at lower temperature, as it is well known in the art that E. coli can be easily cultivated at temperatures at least as low as 4°C. Accordingly, the artisan would have expected to be able to produce large quantities of functional MHC class I molecules at a low cost through use of the combined methods.

3. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Altman et al (Proc. Nat. Acad. Sci. (USA) [1993] 90:10330-10334; of record) in view of Mottez et al (J. Exp. Med. [1995] 181:493-502; U on form PTO-892, newly cited) and Mage et al (Proc. Nat. Acad. Sci. (USA) [1992] 89:10658-10662; 1 on form PTO-1449 filed 11/20/2008, newly cited) as applied to claim 21 above, and further in view of Lone et al (J. Immunotherapy [1998] 21(4):283-294; V on form PTO-892; newly cited).

Altman, Mottez and Mage have been discussed supra.

Mottez does not specifically teach human MHC class I heavy chain or β_2-microglobulin. However, in a continuation of the same work, Lone teaches that the same techniques were applied to human MHC class I heavy chain HLA-A2.1, which was joined via a 15-amino-acid linker to human β_2-microglobulin. Lone teaches that the single chain MHC class I construct folded properly and was functional (Abstract in particular). Lone teaches that the single chain MHC class I construct specifically bound HLA-A2 restricted peptides and induced peptide-specific cytotoxic T cells to proliferate and produce IL-2.

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to substitute human MHC class I as taught by Lone for the murine MHC class I bound to a specific peptide as taught by Mottez. One would have been motivated, with a reasonable expectation of success by the showing of Lone that the human MHC class I complex associated with peptide and activated T cells as well as the murine MHC class I complex did. One would have been further motivated by the teaching of Mottez that single chain MHC class I complexes can be useful for manipulating an immune response, particularly to an antigen that has low affinity for the MHC molecule (page 501, 2nd column in particular).

Conclusion

4. No claim is allowed.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH

shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571)272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D. /PV/
Patent Examiner
December 15, 2008

/Eileen B. O'Hara/
Supervisory Patent Examiner
Art Unit 1644